

- At page 44, line 14, delete "times," and insert --time--.
- At page 48, line 1, delete "HZN-nonapeptied," and insert --H₂N-nonapeptide--.
- At page 48, line 7, delete "trifluoroacetic," and insert --trifluoroacetic--.
- At page 56, line 19, delete "ofl atom at," and insert --of--.
- At page 57, line 5, delete "biding," and insert --binding--.
- At page 57, line 30, delete "submitted," and insert --3: 731-8--.
- At page 58, line 1, delete "(1 g)," and insert --(1 μ g)--.
- At page 58, line 2, delete "(5 g)," and insert --(5 μ g)--.
- At page 58, line 3, delete "(1 M)," and insert --(1 μ M)--.
- At page 58, line 14, delete "However, results were," and insert --Results were also--.
- At page 59, line 5, delete "a cyclopentyl," and insert --~~a~~cyclopentyl sarcosine--.
- At page 59, line 13, delete "only."
- At page 59, line 16, delete "electrophilic."
- At page 59, line 23, delete "bumbed," and insert --bumped--.
- At page 60, line 2, delete "incubaing," and insert --incubating--.

In the claims:

Please amend the claims as follows:

- sub D¹ 1. (Amended) A method for inhibiting [proliferation of] activation of a T cell[s], wherein the T cell or a progenitor cell thereof was engineered *ex vivo* to express a gene encoding a mutated macrolide binding protein (MBP), which method comprises contacting the cell[s] with a macrolide which induces macrolide-dependent inhibition [of proliferation] of activation of the T cell[s].
- C¹
2. (Amended) A method for [selectively] inhibiting transcription of an NF-AT dependent gene[s] in a [hematopoietic] T cell[s], wherein the T cell or a progenitor cell thereof was engineered *ex vivo* to express an MBP gene encoding a mutated macrolide binding protein (MBP) which method comprises contacting the T cell[s] with a macrolide which selectively binds to the altered MBP relative to the wild-type MBP and induces macrolide-dependent inhibition of transcription of NF-AT dependent gene[s] in the T cell[s].
- sub D² 6. (Amended) The method of claim 1 or 2, wherein the MBP gene was introduced into the cell[s] by DNA transfection.
- C²

C2
CONT.

7. (Amended) The method of claim 1 or 2, wherein the MBP gene was introduced into the cell[s] by virus-mediated transduction.

8. (Amended) The method of claim 1 or 2, wherein the MBP gene was introduced into the cell[s] by homologous recombination.

Sub D3
C3.

16. (Amended) A method for selectively inhibiting [proliferation of] T cell activation in a transplanted T cell comprising

- (i) transplanting, into an animal, a T cell[s] or a progenitor cell thereof, which T cell or progenitor cell thereof which [have] has been engineered ex vivo to express an MBP gene encoding a mutated macrolide binding protein (MBP), the mutated MBP having an altered macrolide-binding specificity relative to the wild-type form MBP and
- (ii) administering to the animal an amount of a macrolide sufficient to inhibit [proliferation] activation of the transplanted T cell[s] or progenitor cell thereof, which macrolide selectively induces macrolide-dependent inhibition of [proliferation] activation of the T cell[s] expressing the mutated MBP compared to cells expressing a wild-type form of the MBP.

Sub D4
C4

20. (Amended) The method of claim 16, wherein the MBP gene was introduced into the cell[s] by DNA transfection.

21. (Amended) The method of claim 16, wherein the MBP gene was introduced into the cell[s] by virus-mediated transduction.

22. (Amended) The method of claim 16, wherein the MBP gene was introduced into the cell[s] by homologous recombination.

C5

26. (Amended) The method of claim 16, wherein the transplanted T cell[s] [are] is autologous to the animal.

27. (Amended) The method of claim 16 or 26, wherein the transplanted T cell[s] [are] is present within transplanted bone marrow.

C6

31. (Amended) A method for reducing graft-versus-host disease in an animal by selectively inhibiting [proliferation] T cell activation of a transplanted T cell, comprising

- (i) prior to transplanting [the] a T cell or a progenitor cell thereof, [transducing it] ex vivo engineering the T cell or progenitor cell thereof with a gene encoding a mutated macrolide binding protein (MBP), which is a mutated form of a native protein selected from the group consisting of FKBP and cyclophilin, the mutated MBP having an altered macrolide-binding specificity relative to the wild-type form MBP; and
- (ii) subsequent to transplanting the T cell or a progenitor cell thereof, administering to the animal an amount of a macrolide sufficient to inhibit [proliferation] activation of the transplanted T cell or progenitor cell thereof, which macrolide selectively induces macrolide-dependent inhibition of [proliferation] activation of the

transplanted T cell expressing the mutated MBP compared to endogenous cells of the animal, such that graft-versus-host disease is reduced.

32. (Amended) An expression construct encoding a mutated FRAP, FKBP, cyclophilin or calcineurin, wherein the mutated protein has an altered macrolide-binding specificity relative to its wild-type form and, in the presence of a macrolide to which it binds, induces macrolide-dependent inhibition of [proliferation] activation of a T cell expressing the mutated protein.
33. (Amended) A kit for selectively inhibiting [proliferation] activation of a T cell, comprising
- (i) an expression construct of claim 32 and
 - (ii) a macrolide which selectively binds to the altered protein relative to the wild-type protein and selectively induces macrolide-dependent inhibition of [proliferation] activation of T cells expressing the mutated MBP relative to T cells expressing only the wild-type MBP.

36. (Amended) An isolated population of cells comprising a T cell or progenitor cell thereof, which is transfected with an expression construct of claim 32.

38. (Amended) A method for rendering a T cell susceptible to inhibition of activation by a macrolide, comprising transfecting a T cell[s] *ex vivo* with a nucleic acid encoding MBP to which the macrolide binds selectively relative to the unmodified MBP, which modified MBP retains the ability to cause macrolide-dependent inhibition of [proliferation] activation of the T cell.

Please add new claims 40- 44:

- 40. The method of claim 16, 31, or 38, wherein the mutated MBP is a mutated form of an FK506 binding protein, and the macrolide is an analog of FK506 or rapamycin.
41. The method of claim 16, 31, or 38, wherein the mutated MBP is a mutated form of a cyclophilin protein, and the macrolide is an analog of cyclosporin.
42. The kit of claim 33, wherein the mutated MBP is a mutated form of an FK506 binding protein, and the macrolide is an analog of FK506.
43. The kit of claim 33, wherein the mutated MBP is a mutated form of a cyclophilin, and the macrolide is an analog of cyclosporin.
44. The expression construct of claim 32, which encodes a mutated FKBP or cyclophilin.--

Remarks

Claims 1-27, 29-33, 36, 38 and 39 are currently being examined. Applicants note with appreciation that the claims were found to be free of the art. Claims 1-2, 6-8, 16, 20-22, 26, 27, 31-33, 36 and 38 have been amended. New claims 40-44 have been added. Support for the